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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/155,676	01/04/1999	DAVID WALLACH	WALLACH=21	8997

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BROWDY AND NEIMARK, P.L.L.C.  
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WASHINGTON, DC 20001-5303

EXAMINER
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EPPS FORD, JANET L

ART UNIT	PAPER NUMBER
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1635

DATE MAILED: 06/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/155,676

Applicant(s)

WALLACH ET AL.

Examiner

Janet L. Epps-Ford, Ph.D.

Art Unit

1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 04 April 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 13-16, 20-22, 30, 43-50, 53-60, 62-71, 73-75 and 77-79 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 62 is/are allowed.
- 6) ☒ Claim(s) 13-16, 20-22, 30, 43-50, 53-60, 63-65, 69-71, 73-75 and 77-79 is/are rejected.
- 7) ☒ Claim(s) 66-68 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 19 April 2000 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4-04-05 has been entered.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### ***Drawings***

3. The Examiner approved the proposed Drawing Corrections submitted by Applicants on 4-19-2000.

### ***Specification***

4. The Examiner approved the Substituted Specification submitted by Applicants on 9-10-2001. Additionally, the Sequence Listing submitted by Applicants on 4-04-05, was accepted by the STIC/Biotech Division of the USPTO and entered into the pending sequence database.

### ***Claim Rejections - 35 USC § 101***

5. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. Claims 20, 22, 50, 53-59, 63, 65, 69-71, 73-75, and 77-79 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Art Unit: 1635

Specifically, the scope of the claimed subject matter encompasses polypeptides or nucleic acid sequences that are a product of nature.

***Claim Rejections - 35 USC § 112***

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 30, 45, 47-49, and 64 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. Claim 30 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The method is incomplete since there is no actual step recited in the method for isolating or identifying a polypeptide, the method concludes with extraction of a second hybrid vector from positive transformed cells to obtain a sequence encoding a protein, however there is no step for the isolation or identification of the polypeptide.

10. Claim 45 recites human TRAF2 having the amino acid residues 222-501 of Traf2, however there is no particular sequence recited in the claims such that the ordinary skilled artisan would be able to ascertain which amino acid residues Applicants are referring to. The claim recites human TRAF2, and then refers to “the amino acid residues 222-501 of TRAF2.” It unclear which TRAF2 (i.e. human, murine, or other form of TRAFS) applicants are referring to in the limitation “the amino acid residues 222-501 of TRAF2.” Moreover, the skilled practitioner would not know how to avoid infringement since there is no particular amino acid sequence set forth in the instant claim, such that the ordinary skilled artisan would know which residues 222-

Art Unit: 1635

501 correspond to. Additionally, claim 45 recites “the cellular activity which is changed or mediated by TRAF2,” there is insufficient antecedent basis for this limitation in the claim, such that the skilled artisan would be able to ascertain which particular “cellular activity” Applicants are referring to, in order to avoid infringement.

11. Claims 47-49 and 64 recite “the cellular activity which is changed or mediated by” the polypeptide of claims 53, 62, 69, or NIK. There is insufficient antecedent basis for this limitation in these claims, such that the ordinary skilled artisan would be able to ascertain which “cellular activity” Applicants are referring to, in order to avoid infringement.

***Response to Arguments***

***Claim Rejections - 35 USC § 112***

12. Claims 13-16, 20-22, 43-45, 49-50, 54-55, 59-60, 63, 69 and 77-79 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons of record set forth in the Official Action mailed 9-05-02, and those set forth in the Official Action mailed 6-27-03.

Claim 69 recites a polypeptide that binds to TRAF2 and either inhibits or increases the activity of NF- $\kappa$ B, said polypeptide comprising:

(a) the amino acid sequence of SEQ ID NO: 2, an amino acid sequence encoded by the nucleotide sequence of SEQ ID NO: 6, or the amino acid sequence of SEQ ID NO: 5;

(b) an amino acid sequence of an analog of a), having no more than ten changes in the amino acid sequence of a), each said change being a substitution, deletion or insertion or an amino acid, which analog binds to TRAF2 and either inhibits or increases the activity of NF- $\kappa$ B;

(c) an amino acid sequence of a fragment of a), which fragment binds to TRAF2 and either inhibits or increases the activity of NF- $\kappa$ B; or

(d) a derivative of a), b) or c) by modification of a functional group which occurs as a side chain or an N- or C-terminal group of one or more amino acid residues thereof without changing one amino acid to another of the twenty commonly occurring natural amino acids, which derivative binds to TRAF2 and either inhibits or increase the activity of NF- $\kappa$ B.

Applicant's arguments filed 4-04-05 have been fully considered but are not persuasive. Applicants traverse the instant rejection on the grounds that the "fragments" recited in part (c) of claim 69 should satisfy the written description requirement by the same logic as is set forth in Example 14 of the Examiner Training Materials. According to Applicants, "[j]ust as procedures for making variants that have 95% identity to a sequence and retain its activity are conventional in the art, so are procedures for making fragments of a given sequence that retain their activity. The genus of fragments is not expected to be inordinately large since all of the fragments must possess the specified activity and have a sequence that is a part of the sequence of the polypeptides specifically set forth in paragraph a) of claim 69. The specification teaches how to determine whether any given fragment binds to TRAF2 and either inhibits or increases the activity of NF- $\kappa$ B. Thus, by the same logic as is provided in Example 14 of the Examiner Training Materials, one of skill in the art would conclude that applicants were in possession of the necessary common attributes possessed by the members of genus."

Contrary to Applicant's assertions, the logic provided in Example 14 of the Examiner Training Materials, does not apply in regards to the genus of "fragments" encompassed by the instant claims. The genus of polypeptides of undefined length which comprise a "fragment" of the polypeptides of part (a) of claim 69 is much broader than the genus of polypeptides comprising at least 95% identity to the sequence set forth in Example 14, because the all of the members of the genus in Example 14 shared a significant level of structural similarity (95% identity) to the single disclosed species of SEQ ID NO: 3, and possess a clearly defined function, namely catalyzing the reaction of A to B. However, in the instant case, although each member of the genus of fragments encompassed by the instant claims comprise a "part of" the sequence set forth in part (a) of claim 69, there is no clear structural correlation between the members of the claimed genus and the asserted function. The members of the claimed genus encompass polypeptides that have opposite activity, namely those that either inhibit or increase the activity of NF- $\kappa$ B. The genus of polypeptides comprising fragments having these opposing activities would be expected to be broader than a genus of polypeptides that have the same function, as indicated in Example 14 of the training materials. Therefore, contrary to Applicant's assertions, the logic used in Example 14 of the examiner training materials is not applicable in the instant scenario. Moreover, the genus of "activities" encompassed by the instant claims is so nebulous that the "activities" of NF- $\kappa$ B could possibly encompass a broad range of undefined activities not set forth in the specification as filed, such that the skilled artisan would not be able to discern which particular activity is either increased or inhibited by the claimed polypeptide comprising said fragments.

Moreover, Applicants argue that the claimed fragments only involve deletions from the N or C-terminal, and do not involve substitutions or insertions. First it is noted that the features upon which Applicants are relying, namely that the claimed fragments involve only deletions from the N *or* C terminal, are not recited in the instant claims. Contrary to Applicant's assertions, the term fragment, may comprise as little as two amino acids of the polypeptides recited in part (a) of claim 69, as long as the polypeptide comprises the desired function. The claimed polypeptides may also comprise fragments that are produced from a deletion at both the N and C terminus, as long as the fragments possess the claimed function.

In regards to the Examiner's position that the specification fails to describe the "active fragments" of antibodies encompassed by claims 22 and 50. The examiner withdraws this portion of the rejection as set forth in the Office Action mailed 6-02-04. However, claims 22 and 50 remain rejected since, it remains that the specification as filed does not provide an adequate description of the full scope of the polypeptides encompassed by claims 53 and 69. Therefore, the full scope of polypeptides which are specific to the full scope of polypeptides encompassed by claims 53 and 69 are also not adequately described.

According to Applicants, the length assigned to the fragments of claim 69 is functionally defined. However, as stated previously, as per MPEP § 2163, "[A] biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." Because of the limited structural information provided in regards to which amino acid residues possessing the claimed function of binding TRAF2 and either



Art Unit: 1635

inhibiting or increasing the activity of NF-kB, and the need for experimentation to determine which amino acid fragments of the polypeptides recited in part (a) of claim 69 possess this function, it is concluded that Applicants were not in possession of the full scope of polypeptides comprising a “fragment” of (a) encompassed by claim 69.

Claim 45 recites a method that comprises the use of a polypeptide comprising at least a portion of human TRAF2 having the amino acid residues 222-501 of TRAF2. However, there is no specific amino acid sequence set forth in this claim that corresponds to TRAF2 (claim 45). Therefore, the scope of this claim encompasses TRAF2 proteins, including all allelic and polymorphic variants, including proteins isolated from all species expressing this protein. Additionally, in regards to the “portion” language recited in claim 45, the claim does not indicate the length of said portion, therefore it can read on “portions” of any length, wherein said polypeptide used in the claimed method may comprise any length of said “portions.” The specification as filed does not provide sufficient description, such that the skilled artisan would be able to predict the full scope of polypeptides encompassed by the instant claims.

The claimed genus of polypeptides recited in claim 69 must be tested by trial and error experimentation since there is no direct correlation between the structures of these numerous polypeptides and the recited function. Therefore, since the genus of polypeptides encompassed by claim 69, including polypeptides comprising analogs and fragments thereof are not adequately described, the DNA sequence encoding them as set forth in claims 54-55, and 77-79 are also not adequately defined. Moreover, due to the degeneracy of the genetic code, there are an exponential number of polynucleotides that may function to encode a single amino acid sequence. Additionally, depending upon how a sequence is processed there could be multiple

Art Unit: 1635

introns in the pre-mRNA encoding a polypeptide, the sequence of which cannot be predicted by the structure of the amino acid sequence. Therefore based upon these considerations, the amino acid sequences of the polypeptides encompassed by claim 69, or the amino acid sequences of the polypeptides encompassed by claims 73-75, cannot be used to predict the structures of the full scope of DNA sequences that encode these polypeptides.

Applicant's arguments do not take the place of evidence that Applicant's were in possession of the full scope of the claimed invention at the time of filing of the instant application.

***Status of Applicant Initiated Interference***

13. On 2-09-01 Applicants sought to initiate an interference between the current application and US Patents 5,843,721 and 5,844,073, wherein the proposed count was claim 3 or 4 of US 5,843,721, or claim 54 of the instant application; or all of claims 1-15 of 5,843,721 and at least claim 54 of the instant application. Additionally, in the Remarks section of the reply filed 2-09-01, Applicants stated that claims 65-68 have been added in anticipation of an interference proceeding with US Patents 5,843,721 and 5,844,073. First it is noted that the prior indication of allowability for claim 54 is withdrawn, therefore the initiation of interference proceedings will be postponed until the indication of allowability of all pending claims. If Applicants wish to file a continuation claiming only the allowable subject matter in the instant application, or cancel all non-allowable claims in the instant application, interference proceedings can then be initiated. However, until all issues are resolved in the instant application the prosecution of this application will continue, and the interference initiation will be postponed.

***Conclusion***

14. Claim 62 is free of the prior art, and allowable.
15. Claim 66-68 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Art Unit: 1635

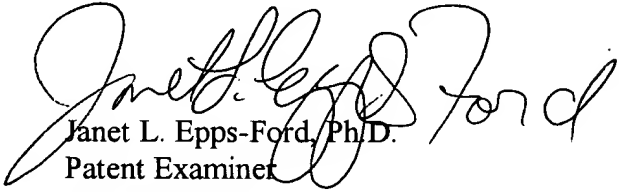
16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford, Ph.D. whose telephone number is 571-272-0757. The examiner can normally be reached on Monday-Saturday, Flex Schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571)272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Janet L. Epps-Ford, Ph.D.  
Patent Examiner  
Art Unit 1635